

WHAT IS CLAIMED IS:

1. A process for preparing an intermediate of zonisamide, comprising the steps of:
 - a) preparing a mixture of chlorosulfonic acid and an organic solvent;
 - b) adding benzisoxazole acetic acid to the mixture;
 - 5 c) heating the mixture; and
 - d) isolating the intermediate of zonisamide.
2. The process according to claim 1, wherein the intermediate of zonisamide is benzisoxazole methane sulfonic acid.
- 10 3. The process according to claim 1, wherein the organic solvent is selected from the group consisting of dichloroethane, dichloromethane, ethylene glycol-dimethyl-ether, toluene and heptane.
- 15 4. The process according to claim 1, wherein the organic solvent is dichloroethane.
5. The process according to claim 1, wherein the benzisoxazole acetic acid is added to the mixture in a molar ratio of benzisoxazole acetic acid: chlorosulfonic acid of about 1:1.3.
- 20 6. The process according to claim 1, wherein the mixture is heated at a temperature between about 0⁰C to about 70⁰C.
7. The process according to claim 1, wherein the isolating step further comprises adding
25 water to the mixture.
8. A process for preparing an intermediate of zonisamide comprising the steps of:
 - a) preparing an acyl sulfate in a solution;
 - b) adding benzisoxazole acetic acid to the solution wherein the benzisoxazole acid is
30 sulfonated by the acyl sulfate to form the intermediate of zonisamide;
 - c) heating the solution; and
 - d) isolating the intermediate of zonisamide.

9. The process according to claim 8, wherein the intermediate of zonisamide is benzisoxazole methane sulfonic acid.
10. The process according to claim 8, wherein the acyl sulfate is formed by preparing a mixture in a solvent, wherein the mixture is selected from the group consisting of an anhydride and sulfuric acid and acyl-halide and sulfuric acid.
11. The process according to claim 10, wherein the acyl sulfate is formed *in situ*.
12. The process according to claim 10, wherein the anhydride is selected from the group consisting of acetic anhydride, propionic anhydride and butyric anhydride.
13. The process according to claim 10, wherein the anhydride is acetic anhydride.
14. The process according to claim 10, wherein the acyl sulfate comprises acetyl sulfate, propionyl sulfate, and butyryl sulfate.
15. The process according to claim 10, wherein the solvent is selected from the group consisting of a polar solvent and a non-polar solvent.
16. The process according to claim 15, wherein the polar solvent is selected from the group consisting of ethylacetate, ethylcellosolve, methylcellosolve, dichloroethane, dichloromethane, chloroform or mixture thereof.
17. The process according to claim 15, wherein the non-polar solvent is selected from the group consisting of toluene, heptane, hexane, alkane or mixture thereof.
18. The process according to claim 15, wherein the solvent is ethyl acetate.
19. The process according to claim 8, wherein the benzisoxazole acetic acid is added to the mixture in a molar ratio of benzisoxazole acetic acid: acyl-sulfate about 1:1 to about 1:1.3.

20. The process according to claim 8, wherein the mixture is heated at a temperature between about 5⁰C to about 150⁰C.
21. The process according to claim 8, wherein the mixture is heated at a temperature between about 5⁰C to about 120⁰C.
22. The process according to claim 8, wherein the mixture is heated at a temperature between about 20⁰C to about 80⁰C.
23. A process for preparing an intermediate of zonisamide comprising the steps of:
- a) preparing a mixture of benzisoxazole acetic acid and an anhydride in a solvent to form a mixture;
 - b) preparing an acyl sulfate in the mixture wherein the benzisoxazole acid is sulfonated by the acyl sulfate to form the intermediate of zonisamide;
 - c) heating the mixture; and
 - d) isolating the intermediate of zonisamide.
24. The process according to claim 23, wherein the acyl sulfate is formed by adding sulfuric acid drop-wise to the mixture containing benzisoxazole acetic acid and anhydride.
25. Benzisoxazole methane sulfonic acid as prepared according to a process of claim 1, wherein the benzisoxazole methane sulfonic acid is substantially free of disulfonated benzisoxazole derivatives.
26. Benzisoxazole methane sulfonic acid as prepared according to a process of claim 8, wherein the benzisoxazole methane sulfonic acid is substantially free of disulfonated benzisoxazole derivatives.
27. Benzisoxazole methane sulfonic acid as prepared according to a process of claim 23, wherein the benzisoxazole methane sulfonic acid is substantially free of disulfonated benzisoxazole derivatives.
28. A crystalline form of benzisoxazole methane sulfonic acid.

29. The crystalline form of benzisoxazol methane sulfonic acid according to claim 28, wherein the crystalline form is at least one of an acid form or a salt form.
- 5 30. The crystalline form of benzisoxazole methane sulfonic acid according to claim 29, wherein the salt form has a metal cation.
- 10 31. The crystalline form of benzisoxazole methane sulfonic acid according to claim 30, wherein the metal cation is selected from the group consisting of sodium, calcium, barium, potassium, magnesium, lithium, manganese, cobalt, iron, copper, nickel, zinc, and silver.
32. A crystalline BOS-Na Form I.
- 15 33. A crystalline BOS-Na Form I, characterized by an X-Ray powder diffraction (XRD) having the main peaks at about 5.0, 17.3, 18.0, 18.6, and 19.7 ± 0.2 degrees two theta.
- 20 34. A crystalline BOS-Na Form I, characterized by an X-Ray powder diffraction (XRD) having the main peaks at about 5.0, 15.7, 16.5, 17.3, 18.6, 19.1, 19.7, 21.5, 22.8, 23.2, 23.5 and 24.3 ± 0.2 degrees two theta.
- 25 35. A crystalline BOS-Na Form I, characterized by a Furier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at about 3546, 3485, 3440, 1641, 669 and 593 cm^{-1} .
- 30 36. A crystalline BOS-Na Form I, characterized by a Furier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at about 3546, 3485, 3440, 1612, 1513, 1439, 1410, 1382, 1234, 1199, 1048, 918, 855, 760, 669 and 593 cm^{-1} .
37. The crystalline BOS-Na Form I as in claim 32, wherein the BOS-Na Form I has a water content of about 7%.
38. A crystalline BOS-Na Form II.

39. A crystalline BOS-Na Form II, characterized by an X-Ray Powder Diffraction (XRD) having the main peaks at about 5.3, 16.6, 21.3 and 26.7 ± 0.2 degrees two theta.
- 5 40. A crystalline BOS-Na Form II, characterized by an X-Ray Powder Diffraction (XRD) having the main peaks at about 5.3, 15.9, 16.6, 21.3 and 26.7 ± 0.2 degrees two theta.
- 10 41. A crystalline BOS-Na Form II, characterized by a Furier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at about 3597 and 3591 cm^{-1} .
- 15 42. A crystalline BOS-Na Form II, characterized by a Furier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at about 3597, 3535, 3496, 3067, 2998, 2951, 1606, 1516, 1438, 1382, 1213, 1064, 1055, 743, 663, 588, 541 and 522 cm^{-1} .
- 20 43. The crystalline BOS-Na Form II as in claim 38, wherein the BOS-Na Form II contains about 1.8% water.
- 25 44. A crystalline BOS-Na Form III.
- 30 45. A crystalline BOS-Na Form III, characterized by an X-Ray Powder Diffraction (XRD) having the main peaks at about 5.0, 5.3, and 17.8 ± 0.2 degrees two theta.
46. A crystalline BOS-Na Form III, characterized by an X-Ray Powder Diffraction (XRD) having the main peaks at about 5.0, 5.3, 15.7, 17.8 and 21.4 ± 0.2 degrees two theta.
47. A crystalline BOS-Na Form III, characterized by a Furier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at about 3604, 1065, 812 and 696 cm^{-1} .
48. A crystalline BOS-Na Form III, characterized by a Furier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at about 3604, 3495, 3067,

2998, 2951, 1605, 1516, 1438, 1382, 1215, 1136, 1065, 1052, 777, 747, 696, 588 and 521 cm^{-1} .

49. A crystalline BOS-Na Form V.

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50. A crystalline BOS-Na Form V, characterized by X-Ray Powder Diffraction (XRD) having the main peaks at about 6.7, 10.9, 16.1, 21.0, 21.2 and 22.2 ± 0.2 degrees two theta.

10 51. A crystalline BOS-Na Form V, characterized by a Fourier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at 3601, 3520, 1587, 1055, 793 and 753 cm^{-1} .

15 52. The crystalline BOS-Na Form V as in claim 49, wherein the BOS-Na Form V has a water content of less than about 1.5%.

53. A crystalline BOS-Ba Form I.

20 54. A crystalline BOS-Ba Form I, characterized by the following X-Ray Diffraction main peaks at about 5.2, 10.4, 12.0, 13.8, 15.6, 17.0, 23.9 and 25.4 ± 0.2 degrees two theta.

25 55. A crystalline BOS-Na Form I, characterized by a Fourier Transform Infra Red Spectroscopy (FTIR) spectrum having the following peaks at about 3544, 3491, 2985, 2943, 1626, 1610, 1509, 1437, 1383, 1369, 1223, 1209, 1175, 1153, 1055, 1043, 911, 869, 752, 651, 603, 543 and 511 cm^{-1} .

56. The crystalline BOS-Ba Form I as in claim 53, wherein the BOS-Ba Form I has a water content about 3.5%.

30 57. A crystalline BOS-Ca Form I.

58. A crystalline BOS-Ca Form I, characterized by having the following X-Ray Diffraction main peaks at about 5.4, 11.7, 16.0, 16.7, 17.7, 18.1, 19.1, 20.8, 24.5, 24.9 and 29.2 ± 0.2 degrees two theta.
- 5 59. A crystalline BOS-H monohydrate Form I.
60. A crystalline BOS-H monohydrate Form I, characterized by having the following X-Ray Diffraction main peaks at about 13.8, 14.4, 17.4, 17.8, 21.8, 22.2, 25.8, 27.8 ± 0.2 degrees two theta.
- 10 61. The crystalline BOS-H monohydrate Form I as in claim 59, wherein the BOS-H monohydrate Form I has a water content about 7.6%.
- 15 62. A process of preparing a BOS-Na Form I, comprising the steps of: 1) preparing a mixture of chlorosulfonic acid in an organic solvent; 2) adding BOA to the mixture; 3) treating the mixture with NaOH to raise pH; and 4) isolating the BOS-Na Form I.
63. The process according to claim 62, wherein the pH is raised to about 10.
- 20 64. The process according to claim 62, wherein the organic solvent is ethyl acetate.
65. A process of preparing a BOS-Na Form I, comprising the steps of: 1) preparing a mixture of an anhydride and sulfuric acid to form acyl-sulfate in the presence of an organic solvent; 2) adding BOA to the mixture; 3) treating the mixture with NaOH to raise pH; 4) cooling the mixture to form a precipitate; 5) drying the precipitate; and 6) keeping the dry precipitate at room temperature to obtain the BOS-Na Form I.
- 25 66. The process according to claim 65, wherein the solvent is ethyl acetate.
- 30 67. The process according to claim 65, wherein the step 6) is performed for about 5 months.

68. A process of preparing a BOS-Na Form II, comprising the steps of: 1) preparing a mixture of an anhydride and sulfuric acid to form acyl-sulfate in the presence of ethyl acetate; 2) adding BOA to the mixture; and 3) treating the mixture with NaOH to raise pH; 4) cooling the mixture to form a precipitate; and 5) drying the precipitate at 80°C to obtain the BOS-Na Form II.
69. A process of preparing a BOS-Na Form III, comprising the steps of: 1) preparing a mixture of an anhydride and sulfuric acid to form acyl-sulfate in the presence of toluene; 2) adding BOA to the mixture; 3) treating the mixture with NaOH to raise pH; 4) cooling the mixture to form a precipitate; and 5) drying the precipitate at 80°C to obtain the BOS-Na Form III.
70. A process of preparing a BOS-Na Form V, comprising the steps of: 1) preparing a mixture of an anhydride and sulfuric acid to form acyl-sulfate; 2) adding BOA to the mixture; 3) treating the mixture with NaOH to raise pH; 4) cooling the mixture to form a precipitate; and 5) drying the precipitate at about 85°C to obtain the BOS-Na Form V.
71. A process of preparing a BOS-Ba Form I, comprising the steps of: 1) preparing a mixture of chlorosulfonic acid and an organic solvent; 2) adding BOA to the mixture; 3) treating the mixture with Ba(OH)₂; and 4) isolating the BOS-Ba Form I.
72. The process according to claim 71, wherein the organic solvent is methylene chloride.
73. A process of preparing a BOS-Ca Form I, comprising the steps of: 1) preparing a mixture of chlorosulfonic acid and an organic solvent; 2) adding BOA to the mixture; 3) treating the mixture with Ca(OH)₂; and 4) isolating the BOS-Ca Form I.
74. The process according to claim 73, wherein the pH is raised to about 12.
75. The process according to claim 73, wherein the organic solvent is methylene chloride.
76. The process according to claim 1, wherein the sodium salt of benzisoxazole methane sulfonic acid is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.

77. The process according to claim 8, wherein the sodium salt of benzisoxazole methane sulfonic acid is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.
- 5 78. The process according to claim 23, wherein the sodium salt of benzisoxazole methane sulfonic acid is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.
79. 1,2-benzisoxazole-3-methane sulfonamide prepared in accordance with the process of claim 76.
- 10 80. 1,2-benzisoxazole-3-methane sulfonamide prepared in accordance with the process of claim 77.
81. 1,2-benzisoxazole-3-methane sulfonamide prepared in accordance with the process of claim 78.
- 15 82. The process according to claim 62, wherein the BOS-Na Form I is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.
83. The process according to claim 65, wherein the BOS-Na Form I is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.
- 20 84. The process according to claim 68, wherein the BOS-Na Form II is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.
- 25 85. The process according to claim 69, wherein the BOS-Na Form III is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.
86. The process according to claim 70, wherein the BOS-Na Form V is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.
- 30 87. The process according to claim 71, wherein the BOS-Ba Form I is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.

88. The process according to claim 73, wherein the BOS-Ca Form I is thereafter converted to 1,2-benzisoxazole-3-methane sulfonamide.